Sleep Medicine 15 (2014) 1398–1404

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Night-time sleep duration and the incidence of obesity and type 2 diabetes. Findings from the prospective Pizarra study

Carolina Gutiérrez-Repiso [a,b,c,*,1], Federico Soriguer [a,b,c,1], Elehazara Rubio-Martín [a,b,c], Isabel Esteva de Antonio [a,b,c], María Soledad Ruiz de Adana [a,b,c], María Cruz Almaraz [a,b,c], Gabriel Olveira-Fuster [a,b,c], Sonsoles Morcillo [a,d], Sergio Valdés [a,b,c], Ana María Lago-Sampedro [a,b,c], Eduardo García-Fuentes [a,b,c], Gemma Rojo-Martínez [a,b,c]

[a] Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM), Spain
[b] UGCI de Endocrinología y Nutrición, Hospital Regional Universitario, Málaga, Spain
[c] Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga, Spain
[d] Diabetes Research Group, Hospital Universitario de Cruces, UPV-EHU, Baracaldo, Spain

ARTICLE INFO

Article history:
Received 13 February 2014
Received in revised form 9 June 2014
Accepted 12 June 2014
Available online 11 August 2014

Keywords:
Night-time sleep duration
Prospective study
Weight gain
Obesity
Type 2 diabetes
Southern Spain

ABSTRACT

Background: Several recent studies have related short sleep duration with different health problems, though the results related with the risk of obesity and type 2 diabetes (T2D) are far from conclusive. The aim of this study was to investigate the association between night-time sleep duration and the incidence of obesity and T2D in a prospective study with a follow-up of 11 years.
Material and methods: The study comprised 1145 people evaluated in 1997–1998 and re-evaluated after 6 years and 11 years. At the three study points, subjects without known diabetes mellitus (KDM) were given an oral glucose tolerance test (OGTT). Anthropometric and biochemical variables were measured. The subjects were asked about their number of hours of night-time sleep.
Results: After adjustment, the OR of becoming obese was significantly higher in subjects who slept ≤7 hours per night, at both the 6-year follow-up (OR = 1.99; 95% CI = 1.12–3.55) and the 11-year follow-up (OR = 2.73; 95% CI = 1.47–5.04). The incidence of T2D at the 6-year follow-up in subjects without T2D at baseline was higher in those who slept ≤7 hours per night (OR = 1.96; 95% CI = 1.10–3.50). However, this association was not independent of obesity, weight gain or abnormal glucose regulation at baseline. At the 11-year follow-up however there was no association between night-time sleep duration and the incidence of T2D.
Conclusions: The incidence of obesity over the 11-year follow-up increased in subjects with fewer hours of night-time sleep. The incidence of T2D according to the hours of night-time sleep depended on obesity and the carbohydrate metabolism phenotype.

1. Introduction

In those countries where sleep duration has been studied, the number of hours of sleep has decreased over recent years [1,2]. This decrease has been related to changes in lifestyle [3]. In recent years, several studies have related short sleep duration with different health problems, in cross-sectional [4–7], prospective [8–10], and intervention studies [11]. However, the particular results related to the risk of obesity and type 2 diabetes (T2D) are far from conclusive [12].

A large cross-sectional study of 375,653 US adults aged ≥18 years (the Behavioral Risk Factor Surveillance System) undertaken in 2009 found a positive association between short sleep duration and the likelihood of having chronic diseases (coronary heart disease, stroke, high blood pressure, asthma, arthritis, T2D and obesity). This association became weaker but did not disappear after adjustment for frequent mental distress (FMD) (FMD ≥14 days during the past 30 days) [4]. Other recent cross-sectional studies found an association between poor sleep quality and short sleep duration and prediabetes and T2D [7,13].

In a large prospective study, the Nurses' Health Study, the authors concluded that the association between a reduced self-reported sleep duration and a diagnosis of T2D could be due to confounding by

* Corresponding author at: UGCI de Endocrinología y Nutrición, Hospital Regional Universitario, Plaza del Hospital Civil, 29009 Málaga, Spain. Tel.: +34 952286704; fax: +34 952286704.
E-mail address: gutierrezrepiso@gmail.com (C. Gutiérrez-Repiso).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.sleep.2014.06.014
1389-9457/

body mass index (BMI), or that sleep restriction may mediate its effects on T2D through weight gain [8]. A recently published systematic review of 13 prospective studies in adults failed to detect a clear association between sleep duration and weight gain [14].

The aim, therefore, of this study was to seek a possible association between night-time sleep duration and the incidence of obesity and T2D at the 6- and 11-year follow-up points in the Pizarra study, a prospective study in progress since 1995 in southern Spain. We examined the hypothesis that those subjects with short night-time sleep duration have a higher risk of becoming obese and/or diabetic.

2. Methods

2.1. Baseline and follow-up studies

This study formed part of the Pizarra cohort study, the characteristics of which have been published previously [15]. In 1997, 1226 subjects were randomly selected from the adult population of Pizarra, a village in the province of Malaga (Spain). The inclusion age was 18–65 years, and individuals were excluded from the study if they were institutionalized for any reason, pregnant, or had a severe clinical or psychological disorder. The final sample distribution, by age and sex, was not significantly different from the population distribution.

The study was approved by the Ethics and Clinical Investigation Committee of Carlos Haya Hospital, and written informed consent was obtained from all participants.

The night-time sleep duration for 1145 subjects was obtained from a self-report questionnaire. Phenotyping of the carbohydrate metabolism was carried out according to the World Health Organization [16] in 1051 of these subjects, performing an oral glucose tolerance test (OGTT) in those subjects who were unaware of their diabetic status.

The cohort was re-evaluated in 2003–2004 (6-year follow-up study). All those who had completed the baseline study were invited by letter or by phone to attend for another clinical and anthropometric examination and another OGTT. In total, 968 of these subjects completed this 6-year follow-up study. In 2009–2010, 673 subjects were re-evaluated (11-year follow-up study).

2.2. Procedures

The protocol was the same at all three study points. The anthropometric study was carried out following a standardized method [17]. At all three study points, measurements were made of weight and height, and the BMI was calculated (weight/height^2). Subjects with BMI >30 kg/m^2 were considered as obese.

The blood glucose level was measured at the three study points using the glucose oxidase method (Accu-Chek, Roche Diagnostics, Barcelona, Spain) at fasting and 120 min after an OGTT with 75 g of glucose. The fasting serum insulin level was measured at baseline and at the 6-year follow-up by radioimmunoassay (Coat a Count RIA kit, DPC, Los Angeles, CA, USA). Insulin resistance was estimated with the HOMA equation (homeostatic model assessment – insulin resistance), as follows: HOMA-IR = [fasting insulin (μU/mL) × fasting glucose (mmol/L)]/22.5.

At all three study points, the blood pressure was measured twice with a sphygmomanometer, with an interval of 5 min between measurements, and the average of the two measurements was used in the analyses. Participants were considered to have hypertension if their blood pressure was ≥140/90 mmHg or if they were receiving antihypertensive treatment.

At all three study points, information on physical activity level, smoking habit, educational level, and other lifestyle habits was obtained using a self-administered questionnaire. Subjects were also asked about night-time sleep duration. The average night-time sleep duration was assessed by asking 'On average, how many hours do you usually sleep at night?' Subjects were divided into two groups according to the night-time sleep duration: those who slept ≤7 h per night and those who slept ≥8 h per night. The cut-off points were the 25th percentile (7 h) and the 50th percentile (8 h) of the frequency distribution. A food frequency questionnaire was completed at baseline and at the 6-year follow-up [18]. The transformation to energy and macronutrients was done by a computer program that included the composition of local foods based on food composition studies [19].

Baseline measurements were made of leptin and interleukin-6 (IL-6). Additional proinflammatory cytokines and adipokines were measured at the 6-year follow-up study: tumor necrosis factor-α (TNF-α) receptors R60KDa (R1) and R80KDa (R2), IL-6, leptin, adiponectin, fatty acid binding protein 4 (FABP4) and high-sensitivity C-reactive protein (hs-CRP). At the 6-year follow-up study, ferritin and resistin were also measured. Ferritin was measured by immunoturbidimetry (ATOM S.A., Barcelona, Spain) using an A15 autoanalyzer from Biosystems S.A. (Barcelona, Spain). Resistin was measured using an enzyme-immunoassay commercial kit (SPI Bio Bertin, York, UK).

Measurements of cytokines were performed using enzyme-immunoassay commercial kits: TNF-α receptors R1 and R2 (BLK Diagnostics, Barcelona, Spain); IL-6 (R&D Systems, Inc., Minneapolis, MN, USA); adiponectin (DRG Diagnostics GmbH, Marburg, Germany); leptin (Mediagnost, Reutlingen, Germany); FABP4 (SPI Bio, Montigny le Bretonneux, France); hs-CRP (BLK Diagnostics).

2.3. Statistical analysis

Data are presented as the mean and standard deviation. Differences between means were calculated using Student's *t*-test or one-way or multivariate analysis of variance. The correlation between variables was measured using Spearman's test. The strength of association between dependent variables and the explanatory variables was measured using logistic regression analysis, calculating the odds ratio (OR) and the 95% confidence interval (CI). In all cases, a rejection level of $\alpha = 0.05$ was used. Analyses were done with SPSS v10 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Population variables according to night-time sleep

The number of hours of night-time sleep decreased over the 11-year follow-up: 8.23 ± 1.30 h (median, 8 h) at baseline, 8.01 ± 1.38 h (median, 7.9 h) at the 6-year follow-up, and 7.18 ± 1.48 h (median, 7 h) at the 11-year follow-up.

Sex, educational level, smoking habit, daily energy consumed, intake of carbohydrates, proteins and lipids, proportion of fatty acids in the diet, hours watching television (TV), dietary habits watching TV, number of meals per day, snacking habits, and alcohol intake (all variables studied on at least one of the three study points) did not vary according to the number of hours of night-time sleep (Table 1).

Subjects who rested ≤7 h per night practised sport in their leisure time less often at both the 6-year ($P = 0.01$) and the 11-year follow-up ($P = 0.02$) (Table 1). On the other hand, daily work activity was described as more intense in those subjects who rested ≤7 h per night at both the 6-year ($P = 0.01$) and the 11-year follow-up ($P = 0.02$), adjusted for age, sex, and obesity (Table 1).

Subjects who drank coffee at least once per day were more likely to sleep fewer hours per night, both at baseline (8.11 ± 1.17 vs 8.43 ± 1.35 h; $P = 0.005$ adjusted for age, sex and obesity) and at the 6-year follow-up (7.82 ± 1.35 vs 8.15 ± 1.40 h; $P = 0.005$ adjusted for

Table 1
General description of the population at the three study points according to the number of hours of night-time sleep.

Characteristics	Baseline			6-year follow-up			11-year follow-up		
	≤7 h (*N* = 300) (26.5%)	≥8 h (*N* = 845) (76.8%)	*P*	≤7 h (*N* = 345) (35.8%)	>8 h (*N* = 623) (64.4%)	*P*	≤7 h (*N* = 376) (55.9%)	≥8 h (*N* = 297) (54.1%)	*P*
Age (years)	38.9 ± 12.2	39.29 ± 14.16	0.80	43.12 ± 11.45	47.90 ± 14.86	0.001	52.75 ± 12.99	50.57 ± 14.01	0.03
Men/women (%)	41.7/58.3	37.8/62.2	0.20[a]	41.7/58.3	34.3/65.1	0.40[a]	31.6/68.4	36.7/66.3	0.35[a]
Educational level (none or until 14 years) (%)	45.3	49.6	0.22[b]	41.6	54.8	0.32[b]	56.4	50.3	0.50[b]
Smoking (yes) (%)	41.0	39.3	0.78[c]	35.1	27.7	0.16[c]	21.1	28.3	0.09[c]
BMI (kg/m^2)	28.23 ± 12.14	27.08 ± 15.10	<0.0001[b]	29.15 ± 5.36	28.33 ± 5.23	0.02[b]	29.58 ± 6.09	28.80 ± 5.55	0.22[b]
Obesity (>30 kg/m^2) (%)	32.7	26.3	0.01[b]	31.9	38.6	0.84[b]	41.7	35.8	0.35[b]
T2D (%)	9.2	14.1	0.05[c]	16.9	22.5	0.04[c]	24.2	22.7	0.81[c]
Hypertension (%)	53.6	54.4	0.80[c]	51.9	61.5	0.26[c]	48.3	45.4	0.33[c]
HOMA-IR[d]	2.50 ± 1.76	2.68 ± 2.27	0.10[c]	2.26 ± 2.38	2.15 ± 1.80	0.86[c]			
HOMA: 75th percentile (%)	21.3	25.9	0.20[e]	36.0	39.0	0.38[e]			
Leisure physical activity (%)	18.1	19.3	0.63	33.7	41.7	0.01[c]	35.9	42.1	0.02[c]
Intense work activity (%)				20.5	10.5	0.01[c]	11.2	8.4	0.02[c]
Intake of macronutrients									
Energy (kJ/day)	2221.17 ± 740.46	2203.51 ± 692.88	0.53[c]	2077.55 ± 823.0	1919.78 ± 659.33	0.23[c]			
Carbohydrates (g)	247.8 ± 12.44	250.32 ± 91.85	0.51[c]	217.06 ± 97.74	197.73 ± 82.20	0.06[c]			
Proteins (g)	84.06 ± 27.05	83.47 ± 27.54	0.44[c]	78.84 ± 37.72	72.43 ± 26.86	0.08[c]			
Lipids (g)	101.67 ± 33.5	99.66 ± 33.45	0.86[c]	99.60 ± 48.03	94.30 ± 43.27	0.91[c]			
Carbohydrates (%)	44.14 ± 7.08	45.14 ± 7.87	0.31[c]	42.04 ± 10.02	41.39 ± 10.43	0.13[c]			
Proteins (%)	15.53 ± 2.89	15.56 ± 3.03	0.71[c]	15.70 ± 5.28	15.42 ± 4.13	0.25[c]			
Lipids (%)	41.85 ± 6.06	40.81 ± 5.82	0.19[c]	42.55 ± 10.31	43.50 ± 10.76	0.07[c]			
Fatty acids (% calories)	9.89 ± 2.18	9.74 ± 2.73	0.99[c]						
MUFA (% calories)	18.44 ± 4.47	18.08 ± 4.11	0.76[c]						
n-6 fatty acids (% calories)	5.13 ± 1.93	4.99 ± 1.77	0.67[c]						
n-3 fatty acids (% calories)	0.45 ± 0.16	0.44 ± 0.18	0.81[c]						
Eating habits									
Hours watching TV				2.01 ± 1.46	2.34 ± 1.48	0.07[b]	1.89 ± 1.26	2.07 ± 1.65	0.22[b]
Eating watching TV (%)				60.6	60.0	0.26	55.3	56.2	0.55
Snacking (%)							13.3	11.1	0.39
≥5 meals per day (%)	1.7	0.8	0.14	6.1	4.5	0.54			
Alcohol intake (%)			0.78			0.10			0.12
Daily	8.9	9.9		9.9	12.9		18.5	18.4	
1–5 times/week	26.6	25.9		26.8	20.6		40.8	30.8	
Never	64.5	65.0		63.2	66.7		59.3	52.2	
Coffee (>1/day) (%)	62.6	51.6	0.002[c]	50.0	40.1	0.03[c]	46.0	45.1	0.89[c]
Decaffeinated coffee (>1/day)				36.0	38.0	0.28	34.1	32.2	0.48
Cytokines and inflammatory markers									
Leptin (ng/mL)	12.35 ± 13.03	11.67 ± 11.52	0.32[c]	13.25 ± 10.94	14.26 ± 1.82	0.98[c]			
IL-6 (pg/mL)	2.15 ± 0.81	2.29 ± 0.65	0.65[c]	2.18 ± 3.49	2.54 ± 4.97	0.54[c]			
R1-TNF-α (ng/mL)				3.12 ± 4.18	3.38 ± 4.37	0.38[c]			
R2-TNF-α (ng/mL)				8.47 ± 10.26	9.81 ± 10.85	0.12[c]			
hs-CRP (mg/L)				1.01 ± 2.42	1.09 ± 2.65	0.62[c]			
Adiponectin (mg/L)				12.27 ± 17.82	11.82 ± 13.61	0.51[c]			
FABP4 (ng/mL)				24.71 ± 14.13	27.80 ± 17.12	0.26[c]			
Ferritin (μg/L)				97.14 ± 94.54	102.06 ± 142.2	0.30[c]			
Resistin (ng/mL)				4.32 ± 1.77	4.49 ± 1.81	0.16[c]			

BMI, body mass index; T2D, type 2 diabetes; HOMA-IR, homeostatic model assessment – insulin resistance; MUFA, monounsaturated fatty acids; TV, television; IL, interleukin; TNF, tumor necrosis factor; hs-CRP, high-sensitivity C-reactive protein; FABP, fatty acid binding protein.

[a] Adjusted for age.
[b] Adjusted for age and sex.
[c] Adjusted for age, sex and obesity.
[d] Excluding those subjects with known T2D.
[e] Adjusted for age, sex, obesity and abnormal glucose regulation (excluding known T2D).

Table 2
Incidence of obesity and risk of becoming obese at the 6-year follow-up points.

Baseline BMI	6-year follow-up			11-year follow-up		
	Night-time sleep duration		Adjusted OR (95% CI)	Night-time sleep duration		Adjusted OR (95% CI)
	≤7 h at baseline	≥8 h at baseline		≤7 h at any of the three study points	≥8 h at any of the three study points	
<30 kg/m^2	18.5%	12.5%[a]	1.99 (1.12–3.55)[b]	28.2%	15.8%[c]	2.73 (1.47–5.04)[d]
>30 kg/m^2	94.5%	86.7%[a]	1.85 (0.51–6.68)[e]	87.3%	88.8%[e]	0.66 (0.20–2.09)[e]

BMI, body mass index; OR, odds ratio; CI, confidence interval.
[a] Unadjusted $P = 0.07$.
[b] $P = 0.01$ adjusted for age, sex, leisure physical activity, and weight gain.
[c] Unadjusted $P = 0.004$.
[d] $P = 0.004$ adjusted for age, sex, leisure physical activity, and weight gain throughout the 11-year follow-up.
[e] Not significant.

age, sex and obesity). However, this difference was not evident at the 11-year follow-up or in those subjects who drank decaffeinated coffee. At baseline and at the 6-year follow-up the proportion of subjects who rested ≤7 h per night was significantly higher in the group of subjects who drank coffee at least once per day (Table 1).

The levels of leptin and IL-6 were not significantly different according to the number of hours of night-time sleep, either at baseline or at the 6-year follow-up. At the 6-year follow-up no significant differences were seen in the levels of hs-CRP, TNF-α receptors R1 and R2, adiponectin, FABP4, ferritin or resistin according to the number of hours of night-time sleep (Table 1).

The BMI was significantly higher in those subjects who slept ≤7 h per night at baseline ($P < 0.0001$) and at the 6-year follow-up ($P = 0.02$), after adjusting for age and sex (Table 1). The unadjusted prevalence of obesity was 27.9% at baseline, 36.2% at the 6-year follow-up and 39.1% at the 11-year follow-up. The highest prevalence at the 11-year follow-up was 41% in the group of subjects who slept ≤7 h per night. After adjusting for age and sex, at baseline the prevalence of obesity was significantly higher in those subjects who slept ≤7 h per night ($P = 0.01$) (Table 1). The prevalence of high blood pressure at the three study points differed significantly according to the night-time sleep duration (Table 1).

The prevalence of T2D (known and unknown) was 14% at baseline, 20.4% at the 6-year follow-up and 23.4% at the 11-year follow-up. At baseline and the 6-year follow-up, the prevalence of T2D was significantly higher in those subjects who slept ≥8 h per night (Table 1). No significant differences were seen according to the night-time sleep duration either at baseline or at the 6-year follow-up (after excluding subjects with known T2D) in the HOMA-IR value or in the prevalence of subjects with HOMA-IR value >75th percentile.

3.2. Incidence of obesity and T2D according to the night-time sleep duration

After adjusting for age, sex, smoking habit, physical activity, and coffee consumption, the OR of becoming obese was significantly higher in subjects who slept ≤7 h per night, both at the 6-year follow-up (OR, 1.99; 95% CI, 1.12–3.55) and at the 11-year follow-up (OR, 2.73; 95% CI, 1.47–5.04). The majority of obese subjects at baseline remained obese at the six-year and 11-year follow-up points, independently of the number of hours of night-time sleep (Table 2).

The incidence of T2D at the 6-year follow-up in subjects without T2D at baseline was higher in those who slept ≤7 h per night (OR, 1.96; 95% CI, 1.10–3.50). However, this association was not independent of obesity, weight gain or abnormal glucose regulation at baseline; when these variables were excluded from the logistic regression model, the significance of the association between night-time sleep duration and incidence of T2D disappeared (OR, 1.51; 95% CI, 0.89–2.84). At the 11-year follow-up, however, there was no association between night-time sleep duration and the incidence of T2D (Table 3).

In those subjects who slept ≥10 h at baseline and through the follow-up, the incidence of obesity and T2D was no higher than in those subjects who slept between 7 and 9 h (data not shown).

3.3. Changes in night-time sleep duration

Subjects who increased their night-time sleep duration by ≥2 h at 6-year follow-up were significantly older (45.9 ± 13.0 vs 39.3 ± 13.5 years; $P = 0.001$) and had higher BMI at baseline (29.2 ± 5.1 vs 27.1 ± 5.1 kg/m^2; $P = 0.009$) and at 6-year follow-up (30.3 ± 5 vs 28.1 ± 5.2 kg/m^2; $P = 0.006$) than those who did not increase their night-time sleep duration.

The prevalence of obesity was higher in those subjects who increased their night-time sleep duration, but the risk of becoming obese was not higher (OR, 1.4; 95% CI, 0.3–7.5; $P = 0.6$) after adjusting for age and sex.

At 6-year follow-up, the percentage of subjects who reduced their night-time sleep duration of ≥2 h was 10.6%. These subjects were older (39.0 ± 13.2 years vs 46.2 ± 13.8; $P \leq 0.001$) and had higher BMI both at baseline (27.3 ± 5.0 vs 28.6 ± 4.9 kg/m^2; $P = 0.014$) and at 6-year follow-up (28.4 ± 5.2 vs 29.8 ± 5.0 kg/m^2; $P = 0.012$) than those subjects who did not reduce their night-time sleep duration.

Table 3
Incidence and risk of becoming diabetic at the 6-year and the 11-year follow-up points.

	6-year follow-up			11-year follow-up		
	Night-time sleep duration		Adjusted OR (CI 95%)	Night-time sleep duration		Adjusted OR (95% CI)
	≤7 h at baseline	≥8 h at baseline		≤7 h at any of the three study points	≥8 h at any of the three study points	
Baseline (excluding T2D)	14.0%	10.2%[a]	1.96 (1.10–3.50)[b]	11.8 %	9.8%[a]	1.28 (0.60–2.69)[c]

T2D, type 2 diabetes; OR, odds ratio; CI, confidence interval.
[a] Unadjusted *P*: non-significant.
[b] $P = 0.02$ adjusted for age, sex, physical activity, smoking habit, weight gain, and abnormal glucose regulation at baseline.
[c] Adjusted *P*: non-significant.

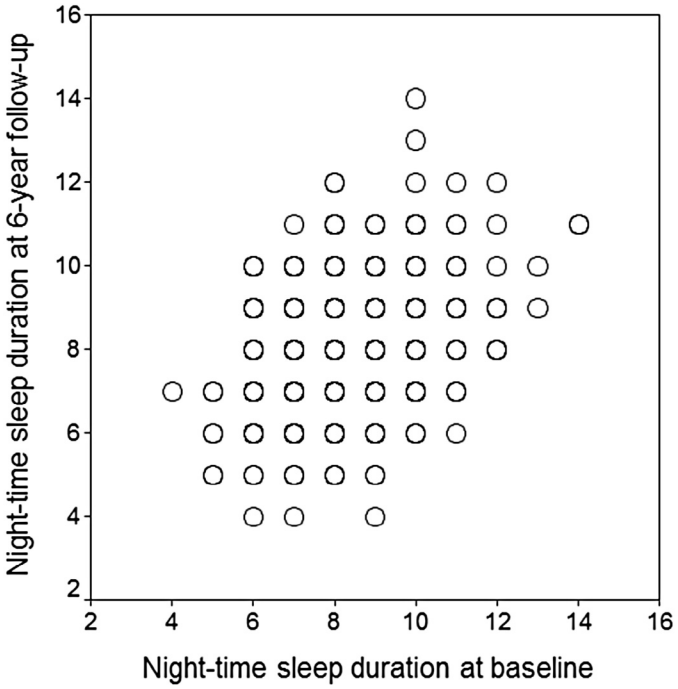

Fig. 1. Correlation plot between night-time sleep duration at baseline and the 6-year follow-up.

In these subjects who reduced their night-time sleep duration, the risk of becoming obese was not significantly different after adjusting for age and sex (OR, 1.3; 95% CI, 0.3–4.8; $P = 0.6$) and excluding obese subjects at baseline.

3.4. Sensitivity analyses

Throughout the 11-year follow-up there were significant correlations between night-time sleep duration at the three study points, between baseline and the 6-year follow-up ($r = 0.31$; $P < 0.001$) (Fig. 1) and between baseline and the 11-year follow-up ($r = 0.25$; $P < 0.001$). The concordance was higher than that due to chance ($P < 0.0001$ between the three study points), but the Kappa index between baseline and the 6-year follow-up (Kappa = 0.25) and between baseline and the 11-year follow-up (Kappa = 0.25) was low. Accordingly, we defined a new variable using hours of night-time sleep at the three study points, establishing four categories of subjects who slept:

(A) ≤ 7 h per night at the three points of the study.
(B) ≤ 7 h per night at baseline and at one of the two follow-up points.
(C) ≥ 8 h per night at baseline and at one of the two follow-up points.
(D) ≥ 8 h per night at all three study points.

After selecting subjects with BMI <30 kg/m^2 at baseline, the incidence of obesity at the 11-year follow-up increased significantly according to the reduction in hours of night-time sleep throughout the whole follow-up of 11 years ($P = 0.02$) (Fig. 2).

Selecting criterion D as the reference criterion and after adjusting for age, sex and weight gain throughout the 11-year follow-up, the OR (95% CI) of becoming obese in group C was 1.14 (0.55–2.39) ($P = 0.71$); in group B it was 2.28 (0.89–5.79) ($P = 0.08$); and in group A it was 3.91 (1.56–9.78) ($P = 0.004$) (P for trend = 0.001).

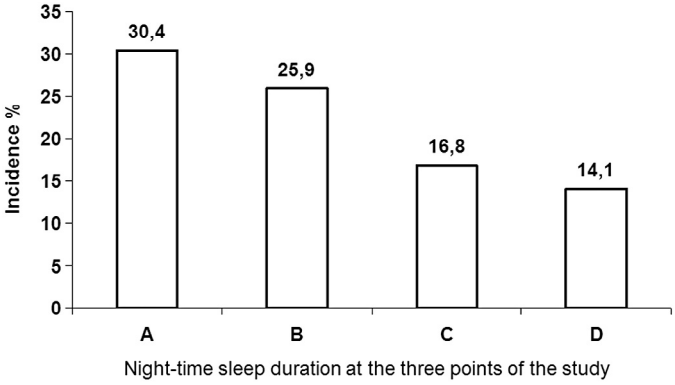

Fig. 2. Incidence of obesity at the 11-year follow-up (excluding subjects with body mass index >30 kg/m^2 at baseline). (A) Night-time sleep duration ≤7 h at all three study points. (B) Night-time sleep duration ≥7 h at baseline and at one of the two follow-up points. (C) Night-time sleep duration ≥8 h at baseline and at one of the two follow-up points. (D) Night-time sleep duration ≥8 h at all three study points.

4. Discussion

The incidence of obesity throughout the 11-year follow-up increased in subjects with fewer hours of night-time sleep, and the difference in the incidence of T2D according to the hours of night-time sleep was not independent of obesity or of the carbohydrate metabolism phenotype.

Several studies in recent years have shown the association between short sleep duration and the risk of obesity [20–22]. Cappuccio et al.'s meta-analysis presented 19 cross-sectional studies in children and 26 in adults [21]. The results showed a consistent pattern of increased odds of being a short sleeper if you are obese, both in childhood and in adulthood. However, the difficulties of observational studies to establish the directionality of the association are well known. Another meta-analysis by Magee and Hale included 13 longitudinal studies in adult persons, finding inconsistent results concerning the relation between sleep duration and weight gain [14]. The differences in design, the age at inclusion, the duration of follow-up, uncontrolled confounding variables or the procedures used to measure night-time sleep duration may be some of the reasons for these differences.

In the Nurses' Health Study, 68,183 women who reported habitual sleep duration in 1986 were followed up for 16 years. The results show that in middle-aged women aged ≤65 years, a habitual sleep duration of <7 h predicts increased future weight gain, independent of baseline weight [23].

Our study was undertaken in a representative sample of men and women from southern Spain. The results show that non-obese subjects who sleep ≤7 h per night had a higher risk of becoming obese throughout the 11-year follow-up period.

The mechanisms whereby short sleep duration may increase the risk of obesity are not clear. A restriction in the number of hours of night-time sleep can increase daily tiredness and reduce physical activity [24]. Other studies found that physical activity increases after brief periods of short sleep duration [25], though others found no change in physical activity [11,23,26]. In our study, subjects who slept fewer hours did less physical activity in their leisure time and their normal daily work was considered more intense.

Several studies have evaluated the relationship between diet and sleep duration. Some have shown that short sleep duration over short periods of time increases food intake [25,27]. Others, however, failed to find this association [24,28]. Some studies have shown that subjects who sleep less consume more fats [24,25,29], fewer vegetables [30] and in general their diet is of a poorer quality [11].

In our study, diet was evaluated at baseline and at the 6-year follow-up. Despite a decrease in daily energy intake, as was expected over the years, neither the total daily energy nor the macronutrients varied according to the number of hours of night-time sleep, either at baseline or at the 6-year follow-up. There were no differences in the habits related to food intake, hours watching TV or alcohol intake according to the night-time sleep duration. Subjects who had coffee at least once per day slept ≤7 h per night. The effect of caffeinated drinks on sleep duration is well known [31], and it was observed at two of the three study points.

Experimental studies in humans have found that short periods of sleep duration result in important changes in the secretion of cortisol, growth hormone [32], and levels of leptin and ghrelin [33], both hormones related to the regulation of hunger and satiety. Changes in the levels of leptin and ghrelin have also been found in cross-sectional studies [34].

The activation of the inflammation cascade due to restriction in sleep duration has been proposed as an intermediary mechanism in the association with obesity [35]. Controlled studies of sleep restriction have found increased levels of TNF-α [36] and IL-6 [36] and decreased levels of leptin [37] and adiponectin [38]. However, in our study, none of the adipokines or inflammatory markers studied at the 6-year follow-up was associated with sleep duration.

In parallel with the association with obesity, we also assessed the association between night-time sleep duration and the prevalence and incidence of T2D, hypertension and insulin resistance, which are all related with obesity. Neither the prevalence and incidence of hypertension nor the prevalence of insulin resistance measured by the HOMA-IR was associated with night-time sleep duration.

The results of the association between the prevalence and incidence of T2D and the night-time sleep duration are paradoxical. In at least two of the study points (baseline and the 6-year follow-up) the prevalence of T2D was lower in those subjects with fewer hours of night-time sleep, but after adjusting for obesity, the incidence of T2D at the 6-year follow-up was significantly higher in those subjects who slept fewer hours. Studies of the association between sleep duration and the risk of T2D show inconsistent results. Several cross-sectional or prospective studies suggest a U-shaped association between sleep duration and T2D [5,6,8,39,40], though others only found the association in women [41]. Cappuccio et al., in a meta-analysis of 10 prospective studies involving 107,756 subjects followed-up for 4.4–32 years and 3586 incident cases of T2D, concluded that the quantity and quality of sleep consistently and significantly predict the risk of the development of T2D [42].

Our study has some limitations. The hours of night-time sleep were measured using questionnaires in which the subjects were asked about hours of night-time resting rather than hours of sleep per 24 h period. At baseline, we noticed that subjects had some difficulty in establishing the difference between the quantity and the quality of the sleep, and also in separating hours of night-time sleep from hours of day-time sleep (for example the afternoon nap), but there was no problem when they were asked about the hours of night-time sleep. In addition, certain common causes of obesity and restriction of sleep duration were not included in our study; for example, psychiatric comorbidities such as depression [43]. Other chronic diseases, physical disability, or use of hypnotics could also be confounders.

There are several definitions of short and long sleepers in literature. The definitions of normal sleep duration ranged greatly across studies varying from 6 h to ≥9 h [44,45]. Some studies have included in the design mid-range sleepers as a reference category (6–8 or 7–8 h), whereas others have not included mid-range sleepers in the comparisons. Also, the proportion of 'natural' short and long sleepers in a population is unknown. These subjects represent a small but significant proportion of the population for whom too much or too little sleep does not seem to be a health problem. These could make the interpretation of the results difficult.

One of the strengths of our study is the evaluation of the night-time sleep duration at the three study points, which showed a positive correlation between the night-time sleep duration throughout the study. In addition, this was a prospective study in which not only night-time sleep duration but also obesity, T2D (using OGTT) and other confounding variables were measured at the three study points.

In summary, the results of this prospective study undertaken in a cohort of subjects in southern Spain support the hypothesis of an association between short sleep duration and the incidence of obesity. This association could be partly explained by the lower level of physical activity undertaken by the subjects with fewer hours of night-time sleep. On the other hand, the association between night-time sleep duration and the incidence of T2D does not seem to be independent of that found with the obesity.

Funding

This study was undertaken with finance from the Fondo de Investigación Sanitaria of the Instituto de Salud Carlos III (PI041883, PI051307, and PI06/90564), Servicio Andaluz de Salud de la Junta de Andalucía (0124/2005 and 0258/2007) and with finance from the Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (CIBERDEM) funds. CIBERDEM is an initiative of the Instituto de Salud Carlos III.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.06.014.

References

[1] Bixler E. Sleep and society: an epidemiological perspective. Sleep Med 2009;10(Suppl. 1):S3–6.
[2] Bin YS, Marshall NS, Glozier N. Secular trends in adult sleep duration: a systematic review. Sleep Med Rev 2012;16:223–30.
[3] Bonnet M, Arand D. We are chronically sleep deprived. Sleep 1995;18:908–11.
[4] Liu Y, Croft JB, Wheaton AG, Perry GS, Chapman DP, Strine TW, et al. Association between perceived insufficient sleep, frequent mental distress, obesity and chronic diseases among US adults, 2009 behavioral risk factor surveillance system. BMC Public Health 2013;13:84.
[5] Gottlieb DJ, Punjabi NM, Newman AB, Resnick HE, Redline S, Baldwin CM, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med 2005;165:863–7.
[6] Chaput JP, Després JP, Bouchard C, Tremblay A. Association of sleep duration with type 2 diabetes and impaired glucose tolerance. Diabetologia 2007;50:2298–304.
[7] Lou P, Chen P, Zhang L, Yu J, Zhang N, Wu H, et al. Relation of sleep quality and sleep duration to type 2 diabetes: a population-based cross-sectional survey. BMJ Open 2012;2(4). pii: e000956.
[8] Ayas NT, White DP, Al-Delaimy WK, Manson JE, Stampfer MJ, Speizer FE, et al. A prospective study of self-reported sleep duration and incident diabetes in women. Diabetes Care 2003;26:380–4.
[9] Gangwisch JE, Steven B, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, et al. Short sleep duration as a risk factor for hypertension: analyses of the first national health and nutrition survey. Hypertension 2006;47:833–9.
[10] Bo S, Ciccone G, Durazzo M, Ghinamo L, Villois P, Canil S, et al. Contributors to the obesity and hyperglycemia epidemics. A prospective study in a population-based cohort. Int J Obes (Lond) 2011;35:1442–9.
[11] Haghighatdoost F, Karimi G, Esmaillzadeh A, Azadbakht L. Sleep deprivation is associated with lower diet quality indices and higher rate of general and central obesity among young female students in Iran. Nutrition 2012;28:1146–50.
[12] Morselli L, Leproult R, Balbo M, Spiegel K. Role of sleep duration in the regulation of glucose metabolism and appetite. Best Pract Res Clin Endocrinol Metab 2010;24:687–702.
[13] Engeda J, Mezuk B, Ratliff S, Ning Y. Association between duration and quality of sleep and the risk of pre-diabetes: evidence from NHANES. Diabet Med 2013;30:676–80.
[14] Magee L, Hale L. Longitudinal associations between sleep duration and subsequent weight gain: a systematic review. Sleep Med Rev 2012;16:231–41.

[15] Soriguer F, Rojo-Martinez G, Almaraz MC, Esteva I, Ruiz de Adana MS, Morcillo S, et al. Incidence of type 2 diabetes in southern Spain (Pizarra Study). Eur J Clin Invest 2008;38:126–33.
[16] Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1998;15:539–53.
[17] World Health Organization Expert Committee. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995;854:1–452.
[18] Soriguer F, Almaraz MC, García-Almeida JM, Cardona I, Linares F, Morcillo S, et al. Intake and home use of olive oil or mixed oils in relation to healthy lifestyles in a Mediterranean population. Findings from the prospective Pizarra study. Br J Nutr 2010;103:114–22.
[19] Mataix J, García L, Mañas M, Martínez-Victoria E, Llopis J. Tabla de composición de alimentos. Granada: Universidad de Granada; 2003.
[20] Patel SR, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity (Silver Spring) 2008;16:643–53.
[21] Cappuccio FP, Taggart FM, Kandala NB. Meta-analysis of short sleep duration and obesity in children and adults. Sleep 2008;31:619–26.
[22] Gangwisch JE, Malaspina D, Boden-Albala B, Heymsfield SB. Inadequate sleep as a risk factor for obesity: analyses of the NHANES I. Sleep 2005;28:1289–96.
[23] Patel SR, Malhotra A, White DP, Gottlieb DJ, Hu FB. Association between reduced sleep and weight gain in women. Am J Epidemiol 2006;164:947–54.
[24] Schmid SM, Hallschmid M, Jauch-Chara K, Wilms B, Benedict C, Lehnert H, et al. Short-term sleep loss decreases physical activity under free-living conditions but does not increase food intake under time-deprived laboratory conditions in healthy men. Am J Clin Nutr 2009;90:1476–82.
[25] Brondel L, Romer MA, Nougues PM, Touyarou P, Davenne D. Acute partial sleep deprivation increases food intake in healthy men. Am J Clin Nutr 2010;91:1550–9.
[26] Benefice E, Garnier D, Ndiaye G. Nutritional status, growth and sleep habits among Senegalese adolescent girls. Eur J Clin Nutr 2004;58:292–301.
[27] Nedeltcheva AV, Kilkus JM, Imperial J, Kasza K, Schoeller DA, Penev PD. Sleep curtailment is accompanied by increased intake of calories from snacks. Am J Clin Nutr 2008;89:126–33.
[28] Weiss A, Xu F, Storfer-Isser A, Thomas A, Ievers-Landis CE, Redline S. The association of sleep duration with adolescents' fat and carbohydrate consumption. Sleep 2010;33:1201–9.
[29] Shi Z, McEvoy M, Luu J, Attia J. Dietary fat and sleep duration in Chinese men and women. Int J Obes 2008;32:1835–40.
[30] Ohida T, Kamal AM, Uchiyama M. The influence of lifestyle and health status factors on sleep loss among the Japanese general population. Sleep 2001;24:333–8.
[31] Butt MS, Sultan MT. Coffee and its consumption: benefits and risks. Crit Rev Food Sci Nutr 2011;51:363–73.
[32] Spiegel K, Leproult R, Colecchia EF, L'Hermite-Balériaux M, Nie Z, Copinschi G, et al. Adaptation of the 24-h growth hormone profile to a state of sleep debt. Am J Physiol Regul Integr Comp Physiol 2000;279:R874–83.
[33] Spiegel K, Tasali E, Penev P, Van Cauter E. Brief communication: sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med 2004;141:846–50.
[34] Taheri S, Lin L, Austin D, Young T, Mignot E. Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index. PLoS Med 2004;1:e62.
[35] Miller MA, Cappuccio FP. Inflammation, sleep, obesity and cardiovascular disease. Curr Vasc Pharmacol 2007;5:93–102.
[36] Vgontzas AN, Zoumakis E, Bixler EO, Lin HM, Follett H, Kales A, et al. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. J Clin Endocrinol Metab 2004;89:2119–26.
[37] Spiegel K, Leproult R, L'Hermite-Baleriaux M, Copinschi G, Penev PD, Van Cauter E. Leptin levels are dependent on sleep duration: relationships with sympathovagal balance, carbohydrate regulation, cortisol, and thyrotropin. J Clin Endocrinol Metab 2004;89:5762–71.
[38] Kotani K, Sakane N, Saiga K, Kato M, Ishida K, Kato Y, et al. Serum adiponectin levels and lifestyle factors in Japanese men. Heart Vessels 2007;22:291–6.
[39] Trenell MI, Marshall NS, Rogers NL. Sleep and metabolic control: waking to a problem? Clin Exp Pharmacol Physiol 2007;34:1–9.
[40] Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. Diabetes Care 2006;29:657–61.
[41] Tuomilehto H, Peltonen M, Partinen M, Seppä J, Saaristo T, Korpi-Hyövälti E, et al. Sleep duration is associated with an increased risk for the prevalence of type 2 diabetes in middle-aged women – the FIN-D2D survey. Sleep Med 2008;9:221–7.
[42] Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care 2010;33:414–20.
[43] Foley DJ, Monjan AA, Izmirlian G, Hays JC, Blazer DG. Incidence and remission of insomnia among elderly adults in a biracial cohort. Sleep 1999;22:S373–8.
[44] Shigeta H, Shigeta M, Nakazawa A, Nakamura N, Yoshikawa T. Lifestyle, obesity, and insulin resistance. Diabetes Care 2001;24:608.
[45] Vioque J, Torres A, Quiles J. Time spent watching television, sleep duration and obesity in adults living in Valencia, Spain. Int J Obes Relat Metab Disord 2000;24:1683–8.